Citation:

He K, Song Y, Daviglus ML, Liu K, Van Horn L, Dyer AR, Greenland P. Accumulated evidence on fish consumption and coronary heart disease mortality: A meta-analysis of cohort studies. *Circulation*. 2004 Jun 8; 109 (22): 2,705-2,711.

PubMed ID: 15184295

Study Design:

Meta-analysis or Systematic Review

Class:

M - Click here for explanation of classification scheme.

Research Design and Implementation Rating:

POSITIVE: See Research Design and Implementation Criteria Checklist below.

Research Purpose:

This meta-analyses aimed to assess the dose-response relation between fish consumption and coronary heart disease (CHD) mortality and to explore major sources of heterogeneity among studies.

Inclusion Criteria:

The criteria for inclusion of studies in the meta-analyses were as follows:

- Studies published between 1966 and 2003 and using prospective cohort study designs
- Studies published only in English
- Relative risks (RR) and their corresponding 95% confident Intervals (CIs) of CHD mortality relating to each category of fish consumption were reported
- Frequency of fish intake was provided (permitted standardizing category of fish consumption).

Exclusion Criteria:

Criteria for exclusion of any study were as follows:

- Of 18 identified studies, five excluded because they were published as short reports
- Two other studies were excluded because they had only two levels of fish intake (yes vs. no or high vs. low)

Description of Study Protocol:

- Relevant observational studies were identified by searching: MEDLINE and EMBASE (1966 to 2003)

- Search terms included "fish," "seafood," "omega-3 fatty acids," "n-3 fatty acids," "cardiovascular disease," "fatal coronary heart disease," and "fatal myocardial infarction" (MI)
- Search was restricted to studies using prospective cohort study design and published in English-language journals
- Papers were included if:
    - RRs and their corresponding 95% CIs of CHD mortality relating to each category of fish consumption were reported
    - Frequency of fish intake was provided, which permitted standardizing categorization of fish consumption
- 13 cohorts, eight included only male participants. Number of participants ranged from 852 in the study by Kromhout et al, to 84,688 in the study by Hu et al, 2002.

Design

Meta-analysis of Cohort studies

Dietary Intake/Dietary Assessment Methodology

- Range of follow-up period: Six to 30 years; average duration of follow-up was 11.8 years
- Data on fish consumption collected using self-administered food-frequency questionnaires (FFQ) (seven cohorts) or in-person interview (six cohorts)
- Fish intake was standardized and classified into five intervals
    - Never or less than one per month
    - One to three per month
    - One per week
    - Two to four per week
    - More than five per week.

Blinding Used

Not applicable.

Intervention

Not applicable.

Statistical Analysis

- Publication bias was assessed by using a Begg's modified funnel plot, in which the RR was plotted on a logarithmic scale against its corresponding SE for each study
- Publication bias was also assessed by two formal tests: The Begg-adjusted rank correlation test and the Egger's regression asymmetry test
- All analyses were performed with the use of the STATA statistical software (Version 7.0, STATA Corp).

Data Collection Summary:

- *Timing of measurements:* Not applicable
- *Dependent variables:* CHD mortality
- *Independent variables:* Fish consumption
- *Control variables:* Fish intake categories.

Description of Actual Data Sample:

- *Initial N:* 13 cohorts, N=222,364
- *Attrition (final N):* Same
- *Age range:* 30-79 years
- *Ethnicity:* Vary
- *Other relevant demographics:* Not applicable
- *Anthropometrics:* Not applicable
- *Location:*
  - USA
  - UK
  - Netherlands
  - Finland
  - Denmark
  - Italy
  - China.

Summary of Results:

- Beneficial effects on CHD mortality gradually increased as a function of fish consumption
- Compared with those who never consumed fish or ate fish less than once per month, individuals who ate fish once per week had significantly lower CHD mortality rates (pooled multivariate RR, 0.85; 95% CI, 0.76 to 0.96)
- Individuals who ate fish five or more times per week, CHD mortality was lower by 38% (RR, 0.62; 95% CI, 0.46 to 0.82)
- In five included studies that presented data on non-fatal MI, pooled RRs across five categories of fish intake were 1.0;0.88 (95% CI, 0.70 to 1.10), 0.95 (95% CI, 0.75 to 1.22), 0.86 (95% CI, 0.67 to 1.09) and 0.79 (95% CI, 0.64 to 0.99; P for trend=0.40) for non-fatal MI.

Variables	Number of Participants (Events)			Fish Consumption		
		Less Than One Per month	One to Three Per month	One Per Week	Two to Four Per Week	At Least Five Per Week
All studies	222,364 (3,032)	1	0.89 (0.79-1.01)	0.85 (0.76-0.96)	0.77 (0.66-0.89)	0.62 (0.46-0.82)
Gender*		1				
Men	89,102 (1,730)	1	0.83 (0.69-1.00)	0.84 (0.72-0.98)	0.72 (0.52-0.98)	0.65 (0.46-0.92)
Women	125,873 (1,055)	1	0.97 (0.82-1.16)	0.84 (0.68-1.05)	0.72 (0.57-0.92)	0.55 (0.33-0.91)

Follow-up <12 years (five studies)	103,218 (1,326)	1	0.96 (0.81-1.14)	0.91 (0.74-1.11)	0.78 (0.62-0.96)	0.69 (0.48-1.00)
Follow-up ≥12 years (11 studies)	119,146 (1,706)	1	0.83 (0.70-0.99)	0.82 (0.71-0.95)	0.69 (0.49-0.97)	0.52 (0.33-0.82)
Diet assessment		1				
Self-administered FFQ (seven studies)	198,708 (1,874)	1	0.94 (0.81-1.10)	0.86 (0.73-1.02)	0.76 (0.63-0.92)	0.64 (0.47-0.86)
In-person interview	23,656 (1,158)	1	0.81 (0.67-1.00)	0.84 (0.71-0.99)	0.77 (0.62-0.96)	0.39 (0.13-1.16)

*Men included six studies with 100% male participants; women included four studies (100%, 62%, 62% and 61% women, respectively) with 88% female participants; Osler's study was not included in either group (women, 47%).

Other Findings

- In stratified analyses, gender did not appear to materially modify the inverse association between fish intake and CHD mortality
- Inverse associations were more evident among those studies with a follow-up of 12 years or longer.

Author Conclusion:

- Authors found a consistently inverse association between fish consumption and CHD mortality rates. The results suggested that eating fishonce per week might significantly reduce death from CHD by 15%
- A dose-response relation was evident between fish consumption and risk of CHD mortality. An increment of 20 g per day of fish intakecould possibly lower CHD mortality rates by 7%
- The inverse association was more apparent among studies with a follow-up period of 12 years or longer. On the basis of the available data, the beneficial effects of fish intake on CHD mortality rates were not materially modified by gender or methods of dietary assessment.

Reviewer Comments:

- *Analyses are based on observational studies, and the inherent limitations of such studies may affect findings. Possibility of residual confounding or bias including measurement errors cannot be excluded*
- *Dietary assessment, the number of exposure categories, and the reference group varied across individual studies and differences might lead to difficulties in estimating the true effect*
- *Results were likely to be affected by misclassification of fish intake*
- *Seven of 18 relevant published studies were excluded, because the presentation of results was too uninformative to allow extraction of a credible effect estimate or weight and the possibility that the findings were affected by the exclusion cannot be completely ruled out.*

Relevance Questions		
1.	Will the answer if true, have a direct bearing on the health of patients?	Yes
2.	Is the outcome or topic something that patients/clients/population groups would care about?	Yes
3.	Is the problem addressed in the review one that is relevant to nutrition or dietetics practice?	Yes
4.	Will the information, if true, require a change in practice?	Yes

Validity Questions		
1.	Was the question for the review clearly focused and appropriate?	Yes
2.	Was the search strategy used to locate relevant studies comprehensive? Were the databases searched and the search termsused described?	Yes
3.	Were explicit methods used to select studies to include in the review? Were inclusion/exclusion criteria specified and appropriate? Were selection methods unbiased?	Yes
4.	Was there an appraisal of the quality and validity of studies included in the review? Were appraisal methods specified, appropriate, and reproducible?	Yes
5.	Were specific treatments/interventions/exposures described? Were treatments similar enough to be combined?	Yes
6.	Was the outcome of interest clearly indicated? Were other potential harms and benefits considered?	N/A
7.	Were processes for data abstraction, synthesis, and analysis described? Were they applied consistently across studies and groups? Was there appropriate use of qualitative and/or quantitative synthesis? Was variation in findings among studies analyzed? Were heterogeneity issued considered? If data from studies were aggregated for meta-analysis, was the procedure described?	Yes
8.	Are the results clearly presented in narrative and/or quantitative terms? If summary statistics are used, are levels of significance and/or confidence intervals included?	Yes
9.	Are conclusions supported by results with biases and limitations taken into consideration? Are limitations of the review identified and discussed?	Yes
10.	Was bias due to the review's funding or sponsorship unlikely?	Yes